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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,207	12/09/2003	D. Wade Walke	LEX-0466-USA	5980
24231	7590	01/13/2005	EXAMINER	
LEXICON GENETICS INCORPORATED 8800 TECHNOLOGY FOREST PLACE THE WOODLANDS, TX 77381-1160			FRONDA, CHRISTIAN L	
			ART UNIT	PAPER NUMBER

1652

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/733,207	<b>Applicant(s)</b> WALKE ET AL.	
	<b>Examiner</b> Christian L Fronda	<b>Art Unit</b> 1652	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) 4 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>12/9/03</u> . | 6) <input type="checkbox"/> Other: ____.  |

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## DETAILED ACTION

### *Election/Restriction*

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
  - I. Claims 1-3 and 5, drawn to an isolated nucleic acid molecule, classified in class 536, subclass 23.1.
  - II. Claims 4, drawn to an isolated oligopeptide, classified in class 530, subclass 350.

2. The inventions are distinct, each from the other because of the following reasons:

The nucleic acid molecule of Group I and the oligopeptide of Group II are patentably distinct products for the following reasons. The invention of Group II is a polypeptide that is composed of amino acids, while the nucleic acid of Group I is a polynucleotide that is composed of purine and pyrimidine units. Polypeptides and nucleic acids are known in the art to be chemically and structurally distinct molecules. While the polypeptide of Group II can be made by recombinant techniques using the polynucleotide of Group I, the polypeptide of Group II can be recovered from a natural source by using protein purification techniques such as affinity chromatography.

Searching the invention of Group I and Group II together would impose a serious search burden. The search of the polypeptide of Group II and the polynucleotide of Group I are not coextensive. The amino acid sequence of the polypeptide of Group II is searched in the amino acid databases while the polynucleotide of Group I is searched in the nucleotide databases. The inventions of Groups I and II have a separate status in the art as shown by their different classifications.

There is search burden also in the non-patent literature. Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to polypeptides which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide but spoke to the gene. Searching in the non-patent literature, therefore is not coextensive. Thus, the search for each of the inventions of Groups I and II requires an extensive analysis of the art retrieved in a sequence search of the appropriate databases and will require an in-depth analysis of technical literature.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and divergent subject matter, and the search required for each group is not required for the other groups because each group requires a different non-patent literature search due to each group comprising different products, restriction for examination purposes as indicated is proper.

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3. During a telephone conversation with David Hibler on 01/04/2005, a provisional election was made without traverse to prosecute Group I, claims 1-3 and 5. Affirmation of this election must be made by applicants in replying to this Office action. Claim 4 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

5. Claims 1-3 and 5, drawn to an isolated nucleic acid molecule are under consideration in this Office Action.

6. Applicants' claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. SEQ ID NOS: 1, 2, and 4 of the instant application have been disclosed in the Sequence Listing of provisional application 60/180,413 filed 02/04/2000.

7. The computer readable form (CRF) of the Sequence Listing dated 12/09/2003 have been received and have been processed by the Scientific and Technical Information Center (STIC).

8. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

***Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph***

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:  
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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In claim 1, line 2, the phrase "24 contiguous bases" renders the claim vague and indefinite because the meaning of the phrase is not known. Amending the claim to recite the phrase "24 contiguous nucleotides" may overcome the rejection. For examination purposes, the claim is assumed to recite "24 contiguous nucleotides".

Claim 2 is vague and indefinite because the claim does not recite the specific stringent hybridization conditions. The metes and bounds of the stringent hybridization conditions cannot be ascertained because the stringent hybridization conditions have widely different interpretations to those skilled in the art in regard to buffer compositions and wash temperature. The claim should be amended to recite the specific buffer compositions and wash temperature in order to define the metes and bounds of the stringent hybridization conditions.

### *Claim Rejections - 35 U.S.C. § 101*

11. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claims 1-3 and 5 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

Applicant discloses the nucleotide sequence of SEQ ID NO: 1 and the deduced amino acid sequences of SEQ ID NO: 2 and SEQ ID NO: 4. Applicants assert that the protein consisting of SEQ ID NO: 2 or SEQ ID NO: 4 is a novel human protein sharing structural similarity with methyltransferase proteins (see specification p. 15, lines 26-29). This is not a specific or substantial utility, but is instead a generic asserted utility. Methyltransferases are known in the art as a diverse group of enzymes with widely differing amino acid sequences, structures, and biological functions having different enzyme classification numbers (see Search in ENZYME for: methyltransferase, Release 36, January 2005, and updates up to 05-Jan-2005; PTO 892).

The specification does not specifically disclose the function or activity of the protein consisting of SEQ ID NO: 2 or SEQ ID NO: 4. The specification does not show any assays that demonstrate that the protein consisting of SEQ ID NO: 2 or SEQ ID NO: 4 has methyltransferase activity. The specification does not disclose that any homology to a reference protein known in the art is a disclosure that the claimed protein automatically has the properties and biological function of the reference protein relied upon.

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The state of the art in protein function prediction from protein amino acid sequence and structure is reviewed by Whisstock et al. (Q Rev Biophys. 2003 Aug;36(3):307-40). Whisstock et al. teach (1) protein function prediction is a difficult problem since homologous proteins often have different and multiple functions; (2) methods for inferring function based on similarity in sequence and/or structure between an unknown protein and one or more well-understood proteins is tenuous and only provide guesses at function; (3) protein function predictions suggest function but do not determine function; (4) the most useful effect of protein function prediction is to guide laboratory experimentation to confirm, refute, or correct the prediction; and (5) protein function prediction from protein sequence and structure is useful but is not a substitute for laboratory experimentation (see entire publication, especially pp. 321-335).

A “specific utility” is specific to the subject matter claimed which contrasts with a general utility that would be applicable to the broad class of the invention. “Substantial utility” is one that provides a specific benefit in currently available form at the time of filing of the invention. Utilities that require or constitute carrying out further research to identify and/or reasonably confirm a specific use are not substantial and do not provide a specific benefit. See MPEP 2107.01

In view of the disclosure and state of the art in protein function prediction stated above, one of ordinary skill in the art would not recognize that claims 1-3 and 5 have a specific or substantial asserted utility or a well established utility since the only recognized utility of the claimed nucleic acid molecule of SEQ ID NO: 1, nucleic acid molecule encoding SEQ ID NO: 2, and nucleic acid molecule encoding SEQ ID NO: 4 is to carry out further research to identify and/or reasonably confirm the specific biological function associated with the claimed nucleic acid molecules.

### ***Claim Rejections - 35 U.S.C. § 112, 1st Paragraph***

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-3 and 5 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know

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how to use the claimed invention.

Furthermore, claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement since the claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The *Wands* factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of claim 2 encompass any isolated nucleic acid molecule of any biological function that hybridizes under any stringent conditions to SEQ ID NO: 1. In order to meet the enablement requirement, one skilled in the art must be able to make and/or use the invention of claim 2 without undue experimentation using the specification coupled with information known in the art. However, neither the specification nor the general knowledge of those skilled in the art provide guidance or prediction on making and/or using the invention of claim 2 without undue experimentation.

The specification discloses the nucleotide sequence of SEQ ID NO: 1 and the deduced amino acid sequences of SEQ ID NO: 2 and SEQ ID NO: 4. However, the specification does not provide guidance, prediction, and working examples regarding the specific nucleotide sequence of any nucleic acid molecule that will hybridize under any stringent conditions to SEQ ID NO: 1 or the specific biological function of the nucleic acid molecule that hybridizes to SEQ ID NO: 1 under any stringent conditions. The general knowledge of those skilled in the art does not provide any guidance or prediction regarding the specific nucleotide sequence of any nucleic acid molecule that will hybridize under any stringent conditions to SEQ ID NO: 1 or the specific biological function of the nucleic acid molecule that hybridizes to SEQ ID NO: 1 under any stringent conditions.

In view of the above considerations, one must perform an enormous amount of trial and error experimentation to make the invention of claim 2. Such trial and error experimentation is well outside the realm of routine experimentation and entails searching and screening for any hybridization condition in which any nucleic acid molecule of any nucleotide sequence can hybridize to SEQ ID NO: 1, searching and screening for any nucleic acid molecule that can hybridize to SEQ ID NO: 1 under selected hybridization conditions, and searching and screening for any biological function for any nucleic acid molecule that hybridizes to SEQ ID NO: 1 under any stringent conditions. Teaching regarding screening and searching for the claimed invention using enzyme assays stated in the specification is not guidance for making the claimed invention.

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The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific hybridization conditions and the specific biological function of any nucleic acid molecule that can hybridize to SEQ ID NO: 1. Without such a guidance, the amount of experimentation left to those skilled in the art to make the invention of claim 2 is undue.

15. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is a highly variant genus claim that is directed toward any isolated nucleic acid molecule comprising at least any 24 contiguous nucleotides of SEQ ID NO: 1 having any biological function.

The scope of claim 1 includes many polynucleotides from many biological sources having widely differing nucleotide sequences; widely differing structural, chemical, and physical characteristics; and widely differing biological functions. Furthermore, the genus is highly variable because a significant number of structural differences between genus members is permitted and genus members have different biological functions.

The specification discloses a polynucleotide of SEQ ID NO: 1 encoding a human protein sharing structural similarity with methyltransferase proteins. However, neither the specification nor the general knowledge of those skilled in the art provide evidence of any description of a structure to function or activity relationship which would be expected to be common to the members of the genus and would distinguish members of the genus from other polynucleotides. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

The disclosed polynucleotide of SEQ ID NO: 1 is not representative of the claimed genus since other members of the genus have widely differing nucleotide sequences and structures and encode proteins with widely differing biological functions. The specification fails to provide a written description of representative polynucleotides as encompassed by the claimed genus.

Since the disclosure fails to describe the common attributes, characteristics, and biological functions that identify members of the genus, and because the genus is highly variant, the disclosed polynucleotide of SEQ ID NO: 1 alone is insufficient to describe the genus. In view of the above considerations, one of skill in the art would conclude that Applicants have failed to sufficiently describe the invention of claim 1 in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of a genus of any isolated nucleic acid molecule comprising at least any 24 contiguous nucleotides of SEQ ID NO: 1

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having any biological function.

Claim 2 is a highly variant genus claim that is directed toward any isolated nucleic acid molecule that hybridizes under any stringent conditions to SEQ ID NO: 1 and has any biological function.

The scope of claim 2 includes many polynucleotides from many biological sources having widely differing nucleotide sequences; widely differing structural, chemical, and physical characteristics; and widely differing biological functions. Furthermore, the genus is highly variable because a significant number of structural differences between genus members is permitted and genus members have different biological functions.

The specification discloses a polynucleotide of SEQ ID NO: 1 encoding a human protein sharing structural similarity with methyltransferase proteins. However, neither the specification nor the general knowledge of those skilled in the art provide evidence of any description of a structure to function or activity relationship which would be expected to be common to the members of the genus and would distinguish members of the genus from other polynucleotides. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

The disclosed polynucleotide of SEQ ID NO: 1 is not representative of the claimed genus since other members of the genus have widely differing nucleotide sequences and structures and encode proteins with widely differing biological functions. The specification fails to provide a written description of representative polynucleotides as encompassed by the claimed genus.

Since the disclosure fails to describe the common attributes, characteristics, and biological functions that identify members of the genus, and because the genus is highly variant, the disclosed polynucleotide of SEQ ID NO: 1 alone is insufficient to describe the genus. In view of the above considerations, one of skill in the art would conclude that Applicants have failed to sufficiently describe the invention of claim 1 in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of a genus of any isolated nucleic acid molecule that hybridizes under any stringent conditions to SEQ ID NO: 1 and has any biological function.

### ***Claim Rejections - 35 U.S.C. § 102***

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use

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or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Stausberg (Accession AA928744).


Claim 1 and 2 are anticipated by Stausberg (Accession AA928744) since Stausberg teach a polynucleotide sequence comprising 152 contiguous nucleotides of SEQ ID NO: 1 which is expected to hybridize to SEQ ID NO: 1 under highly stringent conditions (see attached alignment). Thus, the reference teachings anticipate the claimed invention.

### *Conclusion*

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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